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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/031,562	03/16/93	BOGOCH	S

KRSEK S. EXAMINER, J

18N1/0515

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ART UNIT	PAPER NUMBER
1802	

DATE MAILED: 05/15/96

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Paper No. 31

Serial Number: 08/031,562
Filing Date: March 16, 1993
Appellant(s): Samuel Bogoch

Judith L. Toffenetti
For Appellant

SUPPLEMENTAL EXAMINER'S ANSWER

This is in response to Appellant's reply brief filed February 27, 1996.

(1) *Grouping of claims.*

In response to Appellant's arguments that the argument in rebuttal of the rejections of claims 1 and 2 are broken down into two sections, claims 1 and 2 do not stand or fall together.

It is noted that Appellant's present an argument in this section on page 2 concerning the incorporation by reference of Appellant's application Serial Number 07/744,649 regarding the details of the synthesis of the claimed vaccine. Appellant argues that the details are merely supplemental to the disclosure of the present specification and are not relied upon as essential to the disclosure of the claimed invention, contrary to Examiner's assertion at page 8 of the Examiner's Answer.

It is maintained as set forth on page 2 of the Office Action dated 12/22/93 and in the discussion on page 8 of the Examiner's Answer that the incorporation by reference of the methods of Serial Number 07/744,649 and other Applications is improper of because the methods are not merely supplemental to the disclosure but are considered essential material because without the disclosure of such methods one of skill in the art could not make the claimed vaccine.

(2) *Response to argument.*

The first new ground of rejection which was set forth in the Examiner's Answer and is addressed by Appellant is the following:

The rejection of claim 2 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Appellant makes two statements on page 3 regarding the meaning of the term "immunological specificity". The first statement is that the skilled practitioner in the field of immunology would understand the meaning of this phrase as an art accepted term to mean that **the claimed vaccine is cross reactive with antibodies which recognize and interact with recognin**. The second statement is that the skilled practitioner would recognize this terminology

to mean that **the vaccine product recognizes the antigenic epitope common to malignin, Recognin-L, and Recognin-M**.

These two statements by Appellant do not clarify the meaning of the term "immunological specificity" because the first statement indicates that the claimed vaccine is **a protein which reacts with antibodies which recognize recognin** and the second statement indicates that the claimed vaccine is an **antibody which recognizes the antigenic epitope common to malignin, Recognin-L, and Recognin-M**. While "immunological specificity" may imply that the claimed vaccine is cross reactive with antibodies which recognize recognin, it is maintained that one of skill in the art would not read this term to mean that the vaccine may also be an antibody which recognizes the recognins or malignin. If Appellant intends this phrase to include the limitation of an antibody as a vaccine, it is maintained that the claim is vague and indefinite.

The second new ground of rejection which was set forth in the Examiner's Answer and is addressed by Appellant is the following:

The objection to the specification and the rejection of claims 1 and 2 under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure regarding other Recognins and recognin derivatives.

Appellant argues on page 3, that the data set forth at pages 5 and 6 of the specification clearly shows that three types of cancer cells produce antigenically similar Recognin and that each Recognin produces the same antibody. Appellant argues that the antibody recognized other common cancer cells and therefore, Recognins are distinguished as a family of related antigens. Appellant argues that the Examiner's comments regarding the requirement of undue experimentation to find other Recognins is unfounded, absent some showing that there is reason to believe that all types of cancer do not produce the same Recognin antigen.

While recognin may be present in several types of cancers, as evidence by the production of anti-recognin antibody in the serum of patients with various malignancies, it is maintained that it would require undue experimentation to determine whether these other Recognins would be effective to inhibit or destroy cancer cells upon administration as a vaccine because the properties and specificity of the antibodies generated by the other Recognins is unknown. If the specificity of the antibodies generated by other Recognins is identical to Recognin L, Recognin M, and malignin, it is maintained that it is unpredictable whether administering a Recognin vaccine would be effective in treating the cancer because cancer patients already have increased serum levels of anti-Recognin antibodies, and it is not predictable whether enhancing these antibody levels would be effective in treating the cancer.

On page 4, Appellant describes a method for obtaining antibodies to the 250,000 D precursor protein and a method which was used to determine that a 10,000 D protein contains an epitope of recognin. Appellant states that this method is "described in the prior art relied

upon by the Examiner in making this rejection". Because no prior art was relied upon in the new grounds of rejection, it is not clear to which prior art Appellant is referring. Appellant also states that upon injection, both the 250,000 D precursor protein and the 10,000 D malignin fragment produce the same antibody. Again, it is not clear where this evidence is presented. Assuming that the 250,000 D precursor protein and the 10,000 D protein produce the same antibodies upon injection, it is maintained that the specification does not teach how to make other derivatives of Recognin which produce anti-Recognin antibody. As discussed on page 7 of the Examiner's Answer, it is unpredictable whether the conformation of the epitopes of the Recognin glycoprotein would be maintained in derivatives with additional chemical groups attached to Recognin because the three dimensional structure of these derivatives would be different than the native glycoprotein. Due to the unpredictability concerning the specificity of the antibodies generated by Recognin derivatives, it would require undue experimentation to determine how to make vaccine products or derivatives of Recognin which would contain the immunological specificity of malignin, Recognin L, or Recognin M. For the reasons previously discussed on page 4 of the Examiner's Answer, it would also be unpredictable which derivatives of Recognin or other Recognins would be effective in the treatment of cancer and therefore would require undue experimentation to determine how to make and use these derivatives or other Recognins for the treatment of cancer.

It is noted that the following arguments set forth by Appellant are issues discussed in response to Appellant's initial arguments in the Examiner's Answer. Specifically these arguments relate to the last paragraph of the Examiner's Answer on pages 13-14.

Appellant argues that he is unaware of any antibody that has been demonstrated to actually lyse glioblastoma cells where the antigen in known. Appellant urges that visual evidence is classically relied upon in the field of immunology in showing cell lysis and Appellant's data is consistent with that which is accepted by those of ordinary skill in the art to demonstrate cytotoxicity of antibody. Appellant argues that unless the Examiner is aware of other evidence which shows that this type of data is not reliable in respect to Recognin antibody, this ground of rejection is improper and should be withdrawn.

Appellant's argument has been considered but is not deemed to be persuasive. It is not disputed that the cytotoxicity of recognin antibody has been demonstrated using an art-recognized assay for cytotoxicity (page 8 and Figure 1 of the specification). However, it is maintained that a cytotoxicity assay using one type of cancer cell is not sufficient to demonstrate that the administration of Recognin would result in the treatment of cancer because this *in vitro* assay cannot be extrapolated to the treatment of tumors *in vivo* where other cytokines and cell types which function in the immune response are present, as discussed in the Examiner's Answer on page 13. In addition, other factors such as the anatomical location of the tumor, the tumor mass, and the long tumor-host relationship make the *in vivo* system much more complex and unpredictable.

On pages 5 and 6, Appellant presents an argument using diabetes mellitus as an example of a disease in which the current treatment (i.e the injection of insulin) will extend the individual's life span but will not necessarily control all of the pathological variables of the disease. Appellant argues that the Examiner's requirement that all variables be accounted for in order to demonstrate that a treatment is effective in controlling a particular disease in inaccurate and that intervention in that pathology of a significant variable is routinely accepted as effective treatment of disease.

The discussion on page 13 of the Examiner's Answer did not require that the claimed method control all of the pathological variables of the disease, but rather pointed to the variables which are present *in vivo* that are lacking in an *in vitro* system, thereby preventing the extrapolation from the results of a cytotoxicity assay *in vitro* to the destruction of cancer cells *in vivo*. In view of this point, Appellant's argument concerning diabetes mellitus are not analogous to the above issue. The other evidence listed by Appellant regarding the presence of anti-malignin antibody in individuals with cancer including the actuarial data previously presented, and the *in vitro* cytotoxicity data previously presented has been considered. Each of these issues has been previously addressed. Data regarding presence of anti-malignin antibodies in serum samples is discussed on page 4 and pages 9-12 of the Examiner's Answer, the actuarial data is discussed in detail on pages 9-12 of the Examiner's Answer, and the cytotoxicity data is discussed on page 13 of the Examiner's Answer and is also discussed above.

In conclusion, the sum of the data and arguments presented in response to the previous rejection 35 U.S.C. § 112, first paragraph and the new grounds of rejection set forth in the Examiner's answer are not sufficient to demonstrate that the administration of Recognin or malignin will result in the treatment of cancer for the reasons set forth above.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

JKS

Julie Krsek-Staples, Ph.D.
May 13, 1996

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